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PERFORMANCE DURING EXPOSURE TO IONIZING RADIATION

PART I. FOOD AND WATER CONSUMPTION OF RATS DURING EXPOSURE TO GAMMA RADIATION
PART II. A CONDITIONED AVERSION TOWARDS SACCHARIN RESULTING FROM EXPOSURE TO GAMMA RADIATION

Research and Development Technical Report USNRDL-TR-19
NM 006 015

12 November 1954

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U.S. NAVAL RADIOLOGICAL DEFENSE LABORATORY

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ABSTRACT

The performance of animals during exposure to radiation is under investigation. In Part I of the present report are summarized data concerning food and water consumption and body weight changes occurring during exposure to low intensity gamma radiation. It was found that water consumption was reduced during a single 8-hr exposure to 75 r. The reduction became progressively more severe with repeated exposure to radiation although consumption between exposures was comparable to controls. Food consumption was similarly affected but to a smaller degree. Part II of this report describes a study which demonstrated that the normally high preference of rats for drinking saccharin-flavored water was nullified if this substance was previously associated with radiation exposure. It was concluded that radiation can act as an unconditioned stimulus for altering animal behavior.

SUMMARY

The Problem

To determine the food and water consumption and body changes which occur during exposure to radiation (Part I), and to determine if an animal's behavior towards a normally preferred taste substance can be conditioned by radiation exposure (Part II). Both sets of experiments are presented simultaneously in this report as the initial observations in the study of animal performance during exposure to low intensity ionizing radiation.

Findings

In Part I of this study it was found that food and water consumption was decreased during an 8-hr exposure to low intensity (9.4 r/hr) gamma radiation. The decrease in water consumption became progressively more severe with repeated exposure to radiation. A similar pattern was observed for food consumption but to a lesser degree. Body weight during irradiation reflected the decreased food and water consumption. The decrease in water and food consumption appeared to be restricted to the actual period of exposure since consumption between irradiations was at least that of sham-irradiated controls.

The drinking water available to rats during a 6-hr gamma radiation exposure was made distinctive by addition of saccharin in Part II of this study. Animals irradiated with 30 r or 57 r under these conditions exhibited a marked decrease in their preference for saccharin flavored water during the post-irradiation test. The effect persisted for more than 30 days. It is apparent that animals can learn to discriminate against a normally preferred taste substance when it is associated with radiation exposure.

ADMINISTRATIVE INFORMATION

This work was done as a part of Project Number NM 006 015.04, Phase 11, Technical Objective AW-6.

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PERFORMANCE DURING EXPOSURE TO IONIZING RADIATION

PART I

FOOD AND WATER CONSUMPTION OF RATS DURING EXPOSURE TO GAMMA RADIATION

INTRODUCTION

The effects of radiation upon organisms have been intensively studied during the post-irradiation period. Presumably, these are essentially observations of the recovering animal or of latent manifestations of injury instigated during irradiation. By comparison, relatively little has been reported of the functional changes which may occur during the period of exposure to external radiation. Most experimental data concern changes during exposure to low intensity radiation for an appreciable portion of their lives[1,2] or studies of morbidity during exposure to high intensity X rays.[3,4,5,6]

The present paper describes the marked changes which were observed in food and water consumption and body weight of rats, during an 8-hr exposure to low intensity gamma radiation.

METHODS

Sprague-Dawley rats bred in the Laboratory colony were used throughout the study. Male litter-mates were distributed into experimental and control groups so that each group contained at least one and not more than two members of each litter. All animals were maintained in individual wire cages in air conditioned quarters and received Purina Laboratory Chow ad lib except as noted.

For radiation exposure the animals were confined individually in chambers (7-3/4 by 4-1/2 by 3-1/8 in.) of 1/8 in. Lucite having a lid and false bottom of 1/2 in. wire mesh. The chambers were arranged at isodose

distances around a cobalt-60 "point" source. The radiation source consisted of approximately 7 curies of cobalt-60 contained in a brass capsule of 0.578 in. diameter and 0.812 in. length having a wall thickness of 0.0625 in. A 0.375 in. thick plastic filter surrounded the capsule. The source revolved slowly about its axis during irradiation. Irradiated animals were exposed for 8 hr to a radiation flux of 9.4 r/hr resulting in a total dose of 75 r per exposure. Doses were measured with a Victoreen thimble condenser at the radiation chamber surface nearest the source. The non-irradiated controls were processed identically except that they were sham-irradiated in another room while their litter-mates were being irradiated. Environmental conditions in the radiation and sham-irradiation rooms were similar with respect to temperature, illumination, and noise level.

Food and water were available during irradiation or sham-irradiation except in particular experimental situations described below. A number of food blocks estimated to be more than enough for the requirements of the animal were weighed and placed on the mesh floor of the radiation chamber. At the end of a specified period the food remaining was weighed and the difference termed food consumption. Similarly, water bottles were weighed before and after each period and the difference in these weights used as an index of water consumption. These are estimates rather than absolute measures of food and water consumption since they are not corrected for possible loss through spillage associated with consummatory behavior.*

The amount of food and water consumed during confinement in the radiation chamber was similar to that measured for the same period in the standard maintenance cage.

In three separate experiments, food, water, and body weights were measured immediately prior to radiation exposure, immediately after exposure, and, in the case of experiment A, at various intervals between exposures. Identical measurements were made on their sham-irradiated controls. The second and third experiments were essentially duplications of the original experiment except that water was withheld on alternate radiation exposures. The latter two studies were performed essentially to check the reliability of the observed phenomena.

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*Water spillage was negligible; food spillage measured on 10 normal animals averaged 19 ± 2 per cent during an 8-hr period.

RESULTS

In all three studies consumption of water (Fig. 1) and food (Fig. 2) was decreased during each 8-hr exposure to gamma radiation. The difference in water scores between sham-irradiated and irradiated animals became greater with repeated exposure; during the 5th, 6th, 7th, and 8th exposures the water consumption of irradiated animals was always less than 2 gm per exposure. In contrast, the sham-irradiated controls consumed 10 to 15 gm of water during the same exposure periods. The decrease in water consumption is a relatively sensitive response and is readily observed during a single exposure to 75 r. An analysis of variance was performed on the combined results of the three experiments for the initial radiation exposure and the difference between the water consumption of sham-irradiated and irradiated animals was found to be highly significant ($p < 0.001$).

A similar probability value was obtained for the difference in food consumption scores between sham-irradiated and irradiated animals for a single exposure to gamma rays (exposure no. 1). In the first experiment there was little effect of repetitive exposure upon the amount of food consumed; however, in the second and third experiments the decrease in amount of food consumed was related to the number of radiation exposures (Fig. 2).

The body weight changes during the exposure period appeared to reflect the consumption of water and food. Sham-irradiated animals generally gained weight while irradiated animals lost several grams during each exposure (Fig. 3).

The water and food consumption of animals in experiment A were measured for several periods following each radiation exposure in order to determine the duration of time over which changes in consumption were manifested. The consumption for a 10.2-hr period beginning one hour after each exposure are summarized in Fig. 4. There was no obvious effect of irradiation upon food consumption during this period. Also, there was no difference in water consumption immediately following the first exposure. However, with repeated exposure the water consumption immediately following irradiation increased markedly. The method of supplying water was inadvertently altered for the fifth observation period which may have resulted in a spurious estimate (Fig. 4).

Water and food consumption for consecutive periods during the week following the first and the last exposures are summarized in Table 1. Water consumption was not significantly changed following the first exposure, however following the eighth exposure water consumption of irradiated animals was increased for the entire period. Food intake of

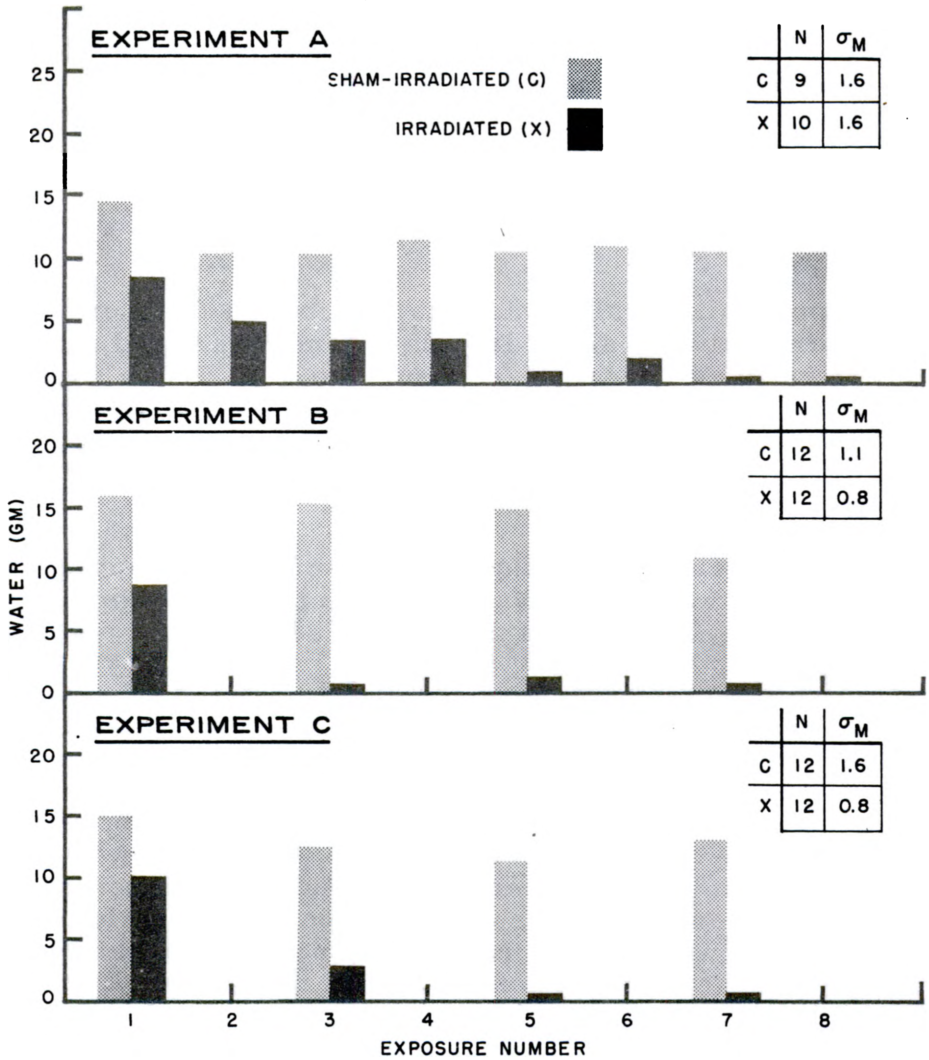

Fig. 1 Mean Water Consumption During Consecutive Weekly Gamma Radiation Exposures in Three Experiments. The Standard Error of the Mean is Given for the Initial Exposure.

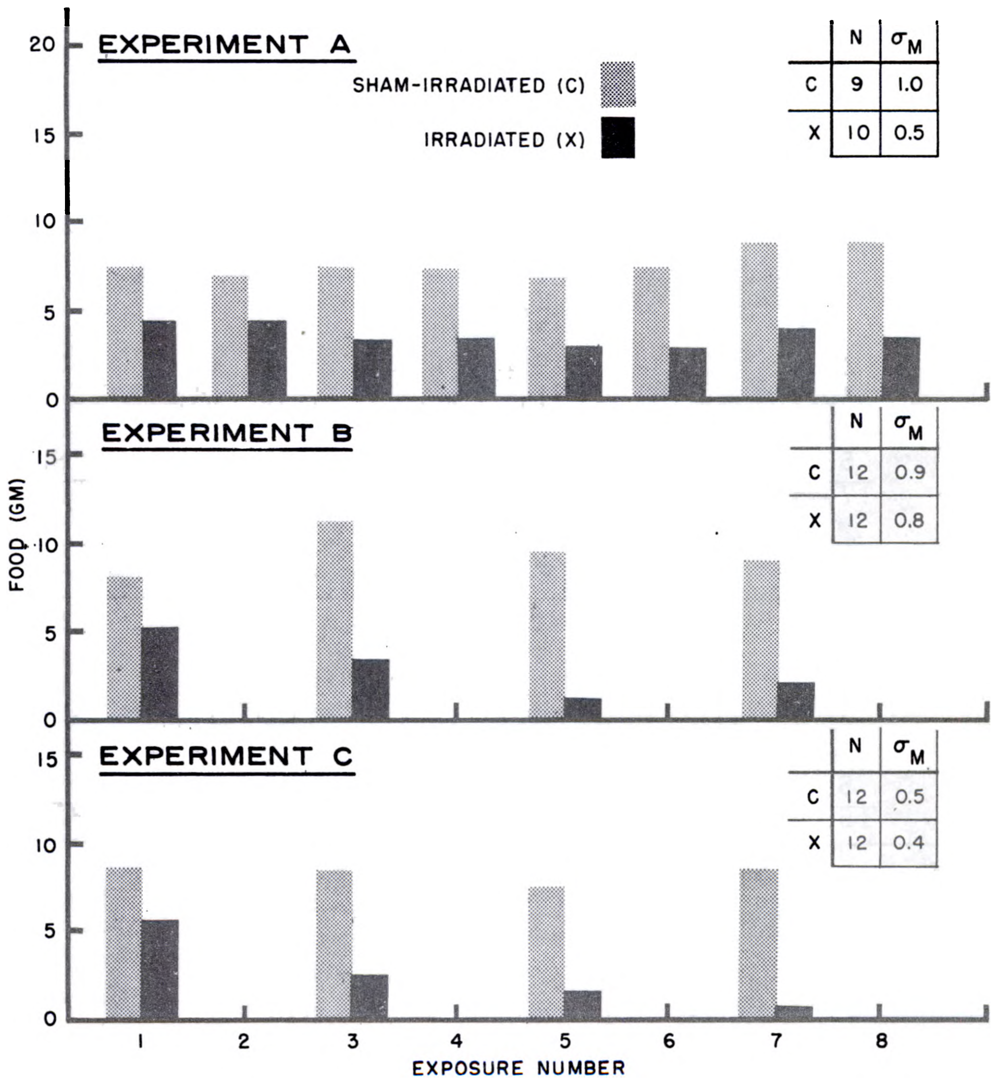

Fig. 2 Mean Food Consumption During Consecutive Weekly Gamma Radiation Exposures in Three Experiments. The Standard Error of the Mean is Given for the Initial Exposure.

TABLE 1

Food and Water Consumption During Consecutive Intervals of Time for the Week Following the First and Eighth Exposure Period. Measurements Began One Hour After Completion of Exposure

Duration of Consecutive Periods (hr)	Exposure No. 1 Sham Irrad.		Exposure No. 1 Irrad.		Exposure No. 8 Sham Irrad.		Exposure No. 8 Irrad.	
	Water Consumption (gm)							
3.4	3.4	(0.5)[a]	3.3	(0.9)	10.0	(0.9)	16.2	(1.4)
6.8	4.5	(0.8)	5.3	(0.8)	7.8	(1.2)	14.8	(3.3)
13.7	21.0	(1.1)	19.7	(1.5)	30.5	(3.4)	30.4	(6.1)
27.5	30.9	(1.9)	31.6	(1.9)	48.7	(4.2)	61.8	(6.1)
54.8	61.1	(3.1)	61.1	(2.6)	74.9	(3.7)	90.2	(4.8)
52.8	53.1	(3.0)	59.9	(3.1)	68.3	(3.4)	76.6	(4.0)
159.0[b]	174.5		180.9		240.2		290.0	
	Food Consumption (gm)							
3.4	1.4	(0.4)[a]	1.3	(0.4)	4.8	(0.3)	5.5	(0.6)
6.8	4.5	(0.5)	4.3	(0.8)	7.1	(0.7)	6.1	(1.0)
13.7	15.7	(0.5)	16.7	(1.2)	15.6	(1.0)	16.4	(1.8)
27.5	26.7	(1.2)	27.9	(1.2)	30.9	(1.2)	31.4	(1.5)
54.8	49.7	(0.4)	49.9	(0.3)	58.0	(2.0)	59.0	(2.4)
52.8	54.4	(2.0)	56.6	(2.0)	58.9	(1.8)	59.9	(2.6)
159.0[b]	152.4		156.7		184.3		181.9	

(a) Standard error of mean
(b) Cumulative total

irradiated animals was not different from that of sham-irradiated controls following either exposure.

The possibility was considered that the decreased water consumption which occurred during irradiation may be responsible for the decreased food consumption. Irradiated and sham-irradiated groups were supplied with food but deprived of water during alternate irradiations of experiments B and C. The results are summarized in Fig. 5. Although water deprivation depressed the food consumption of both groups the irradiated animals continued to consume significantly less food than did sham-irradiated controls.

DISCUSSION

A transient decrease in food consumption in several species of animals has been observed immediately following X irradiation.[7,8,9,10] Presumably, this phenomenon is related to disturbances in gastro-intestinal function occurring during the same time interval. For example, the gastric emptying time in rats has been observed to be prolonged markedly during this period.[11,12] Functional changes in the gastro-intestinal tract occur very early in the radiation syndrome. An increase in intestinal motility and tonus have been observed to occur in rabbits[13] and rats[14] during the period of exposure to X rays. It appears reasonable to assume that the observations of the present study are referable to disturbances in gastro-intestinal function. On the basis of pharmacological studies, Conard[14] concluded that the changes in intestinal motility of rats occurring during irradiation are through the action of X rays upon cholinergic nerves in the intestine. Likewise, Toyama[13] was able to increase intestinal motility of the rabbit by irradiation of autonomic nerve centers and by local irradiation of the intestine.

While food consumption was depressed during exposure there was no evidence of post-irradiation anorexia generally observed in X irradiated rats.[8] It may be that the radiation exposure dose in the present circumstances is insufficient to prolong the decreased consumption beyond the period of exposure. However, it is also possible that the decreased consumption during irradiation is independent of the post-irradiation anoretic phase and is confined to the period of exposure.

The decrease in water consumption became progressively more severe with repeated exposure to radiation. This observation is difficult to interpret simply on the basis of an accumulative effect since water

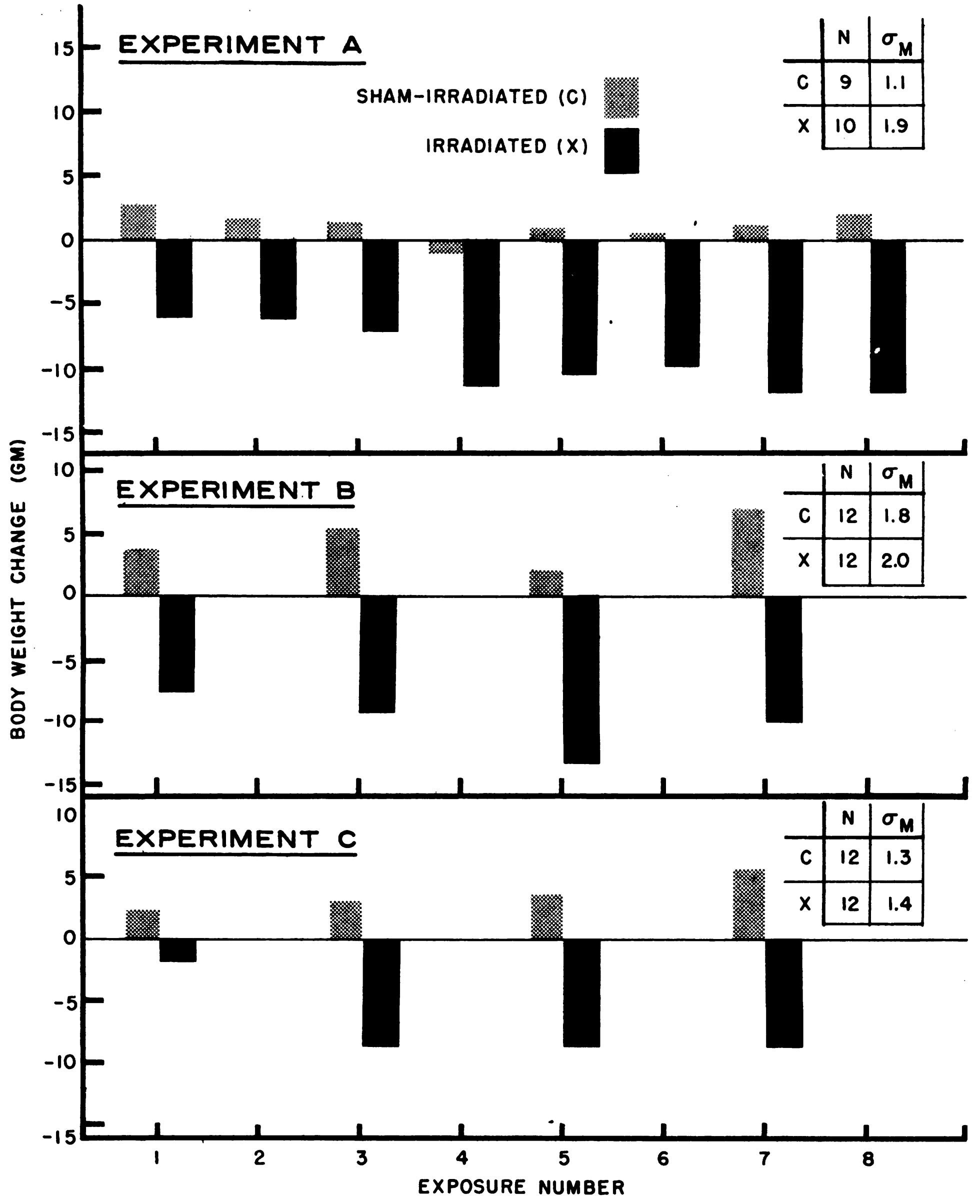

Fig. 3 Mean Change in Body Weight During Consecutive Weekly Gamma Radiation Exposures in Three Experiments. The Standard Error of the Mean is Given for the Initial Exposure.

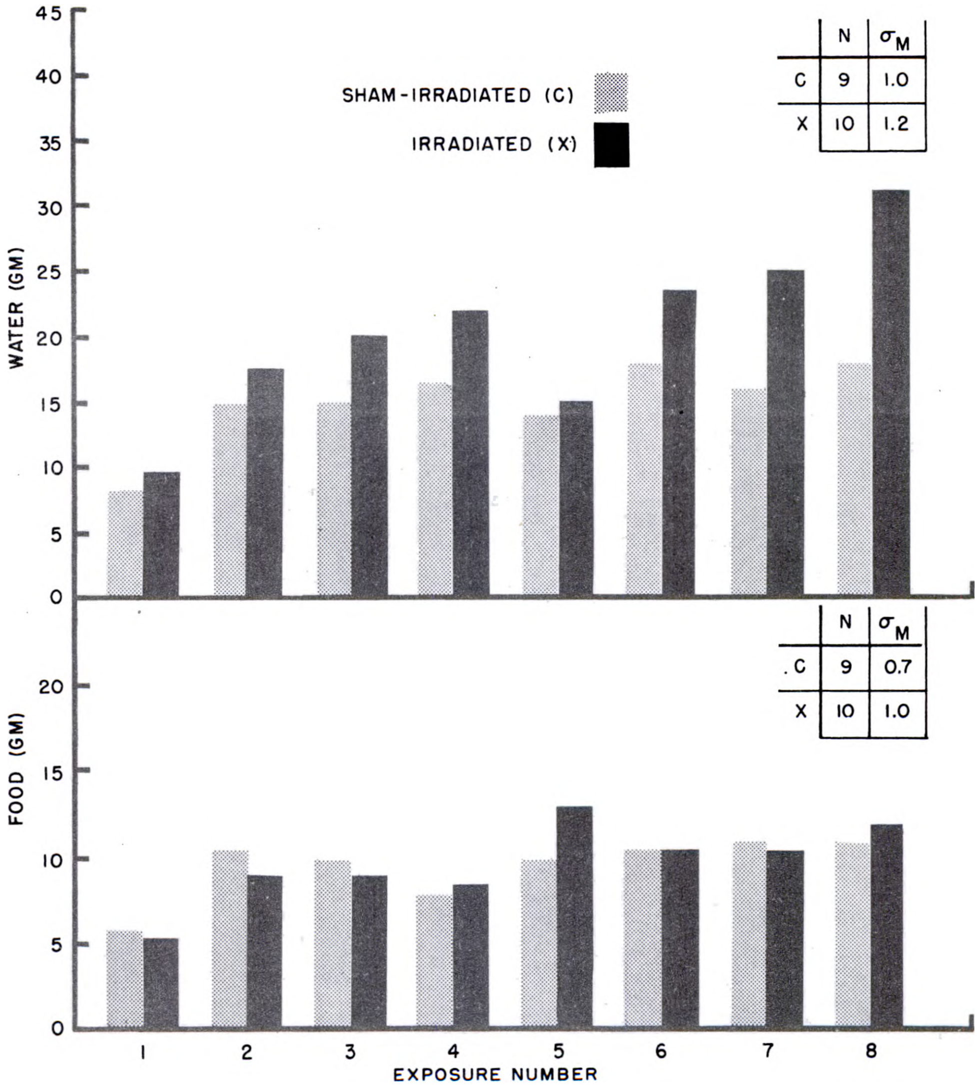

Fig. 4 Mean Food and Water Consumption During 10.2 Hr Following Each Exposure. Measurements Began 1 Hr After Completion of Exposure. The Standard Error of the Mean is Given for the Initial Observation Period.

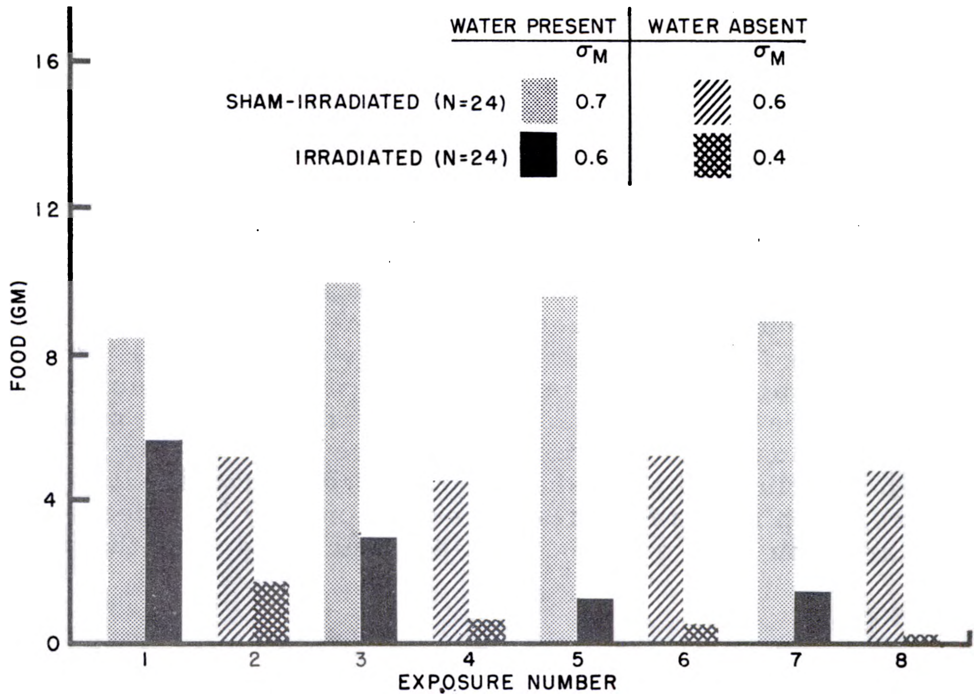

Fig. 5 Mean Food Consumption of Irradiated and Sham-irradiated Animals Deprived of Water During Alternate Gamma Radiation Exposures. The Standard Error of the Mean is Given for the First Exposure (with water present) and the Second Exposure (with water absent).

consumption between exposures was not reduced. On the contrary, water consumption between exposures was increased markedly above that of controls with repeated exposures, indicating that the requirement for water probably was not less than that for non-irradiated animals. In a similar manner the degree of decrease in food consumption appeared to be related to the number of exposures in two of the three experiments.

The change in degree of response with repetitive exposure is suggestive of a conditioned response in which the depression of water and food consumption is strengthened by learning through repeated coupling with the radiation situation. Experiments have been made to determine if stimuli associated with radiation exposure can evoke a conditioned response in the behavior of the animal (Part II).

SUMMARY

During protracted exposure to low intensity gamma radiation there is a decrease in food and water consumption as well as a loss in body weight. The effect is apparent during a single 8-hr exposure to 75 r. The decrease in water consumption becomes progressively more severe with repeated exposure to radiation. Two of three experiments indicate that food consumption also becomes altered according to the number of exposures. The decrease in water and food consumption appears to be restricted to the actual period of exposure since consumption between irradiations is at least that of sham-irradiated controls. It is suggested that the changes in food and water consumption may be referable to the effects of radiation upon gastro-intestinal function during the period of exposure.

PERFORMANCE DURING EXPOSURE TO IONIZING RADIATION

PART II

A CONDITIONED AVERSION TOWARDS SACCHARIN RESULTING FROM EXPOSURE TO GAMMA RADIATION

INTRODUCTION

It was observed previously (see Part I of this report) that the food and water consumption of rats was depressed during exposure to a relatively low dose of low intensity gamma radiation. The severity of this depression increased with successive exposures to radiation although consumption between exposures was similar to or exceeded that of non-irradiated controls. It was suggested that the progressive change in consummatory behavior during repetitive exposures may be, in part, a conditioned response in which the avoidance of water and food is strengthened by learning through repeated coupling with the radiation situation.

A clearer demonstration of the learning phenomenon would be provided if the conditioned avoidance of water or food could be elicited in the absence of radiation exposure. The present report describes the results of an experiment designed to provide such a test. The water available during irradiation was made discriminative to the animal by addition of saccharin. Subsequently, the saccharin flavor was employed as a taste stimulus in a post-irradiation test for a conditioned aversion to the discriminative fluid.

PROCEDURES

The animals were Sprague-Dawley stock bred at this Laboratory. Each animal was maintained in an individual cage. Two plastic 100 cc drinking bottles with glass nipples were attached to each cage except during

specified periods described below. The difference in weight of each drinking bottle and its contents before and after a given test period was used as the estimate of fluid consumption.

Eighty male rats from 16 litters were subjected to a pre-irradiation series of tests to determine their degree of preference for 0.1 per cent saccharin solution with respect to tap water. Both fluids were presented concurrently. Tests were also made to evaluate a possible position preference in drinking in the two-bottle situation. Very few animals exhibited a drinking bottle position preference strong enough to overcome their preference for saccharin. From these tests 20 animals having the lowest preference to saccharin solution and/or highest position preference were eliminated. The remaining animals were randomly assigned to 6 groups with the restriction that each group contain at least one and no more than two members from each litter.

The experimental treatment for each group was as follows:

Group	No. of Animals	Radiation Exposure Dose (roentgens)	Fluid Present During Exposure
I	10	0	Tap Water
II	10	0	Saccharin Solution
III	10	30	Tap Water
IV	10	30	Saccharin Solution
V	10	57	Tap Water
VI	10	57	Saccharin Solution

For radiation exposure all animals were confined in Lucite boxes and exposed in the gamma field of a 7-curie cobalt-60 radiation source. Attached to each box was a single plastic drinking bottle containing either tap water or saccharin solution as specified in the experimental design. The 30 r and 57 r exposures were made at radiation intensities of 5.0 r/hr and 9.5 r/hr, respectively. The sham-irradiated groups were placed in the radiation field behind a lead shield. The total exposure period was 6 hr for all groups. Details concerning the radiation procedures and source have been described in Part I of this report.

Measurements of fluid consumption indicated that all animals had tasted the fluid presented to them during radiation exposure. On day 1 post-irradiation the groups which had received water during exposure were presented with saccharin solution, only, for 6 hr while the other groups received water, only, in order to equalize the experience with saccharin. On day 2 post-irradiation, saccharin solution and water were simultaneously available to each animal for a 6-hr period. Beginning with the third day post-irradiation both saccharin solution and water were available to each animal on a continuous basis. Measurements of consumption were made at 24-hr intervals.

During the post-irradiation preference testing period the drinking bottles were reversed daily to avoid a stereotyped position response. An effect of position was not detectable when the saccharin preference was distinctively high or low. However, when the scores were in the neutral range of preference a position effect could be detected. In order to minimize the effect of position upon the scores each consecutive left and right measurement pair are combined for each animal and 48-hr values reported.

The saccharin preference score utilized is the quotient for the ratio:

$$\frac{\text{Saccharin solution intake (gm)}}{\text{Total fluid intake (gm)}} \times 100.$$

RESULTS

The median pre-irradiation saccharin score for all animals was 86.1 (S.E. = 1.0) for two 6-hr test periods, i.e. saccharin solution constituted 86.1 per cent of the total fluid consumption. The results of the initial post-irradiation preference test period for each group are summarized in Table 2. Animals presented with saccharin during the sham-irradiation (0 r) maintained their preference during the post-irradiation test period. However, animals which were exposed to 30 r or 57 r with saccharin available during irradiation exhibited a marked decrease in their preference score in the post-irradiation test (Table 2). Exposure to 30 r was sufficient to negate the previous preference for saccharin while exposure to 57 r resulted in a striking aversion to saccharin.

The consumption of saccharin and tap water was determined daily for 20 days and then at intervals of 2 to 5 days during the next 40 days. The saccharin preference scores for groups having saccharin available during irradiation are summarized graphically in Fig. 6. The conditioned aversion towards the discriminate fluid was still present 30 days after irradiation although some extinction was apparent.

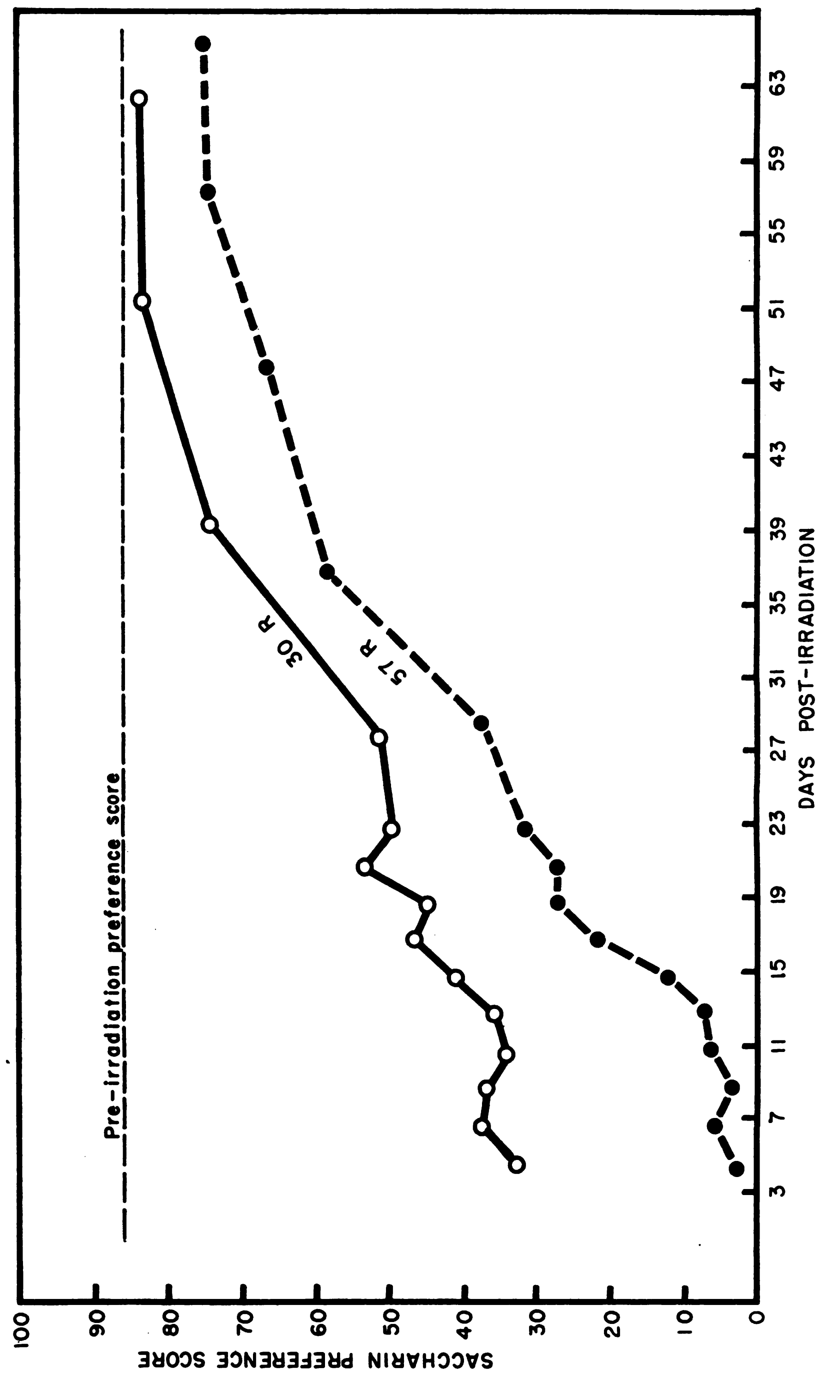

Fig. 6 Median Saccharin Preference Scores for Animal Groups Exposed Concurrently to Gamma Radiation and Saccharin Flavored Drinking Water.

TABLE 2

The Median Saccharin Solution Preference Score for Each Group During the Initial 48-hr Post-irradiation Test Period

Radiation dose (roentgens)	Per Cent of Total Fluid Consumption During Initial 48-hr Post-irradiation Test: Groups II, IV, VI (Saccharin present during irradiation)		Groups I, III, V (Water present during irradiation)	
0	88.0	(11.0)[a]	93.2	(2.3)
30	33.4	(9.8)	94.8	(8.2)
57	3.1	(3.7)	96.8	(1.8)

(a) Standard error of the median

DISCUSSION

The use of saccharin solution in the present study has made it possible to demonstrate the effectiveness of ionizing radiation to act as an unconditioned stimulus in animal behavior. Rats tend to avoid a taste stimulus which has been associated with radiation exposure, although the stimulus is normally preferred. The conditioned aversion to saccharin is relatively radiosensitive being effected by a 6-hr coupling with a 30-r dose of low intensity (5 r/hr) gamma radiation. The conditioning appears to be dose-dependent in terms of the strength of saccharin aversion and in the persistence of this aversion.

Although the conditioned aversion in the present study is dependent upon taste discrimination it may be symptomatic of broader behavioral disturbances instigated during radiation exposure. If this is true then it should be possible to detect avoidance behavior with stimuli other than taste. Such studies are now in progress.

The processes through which radiation is capable of operating as an unconditioned stimulus are unknown. Since consummatory behavior is partially a reflection of gastric function it is plausible to suspect gastro-intestinal disturbances as the physiological events which motivate the animal in the learning situation. Gastro-intestinal functions are known to be disturbed during irradiation and are responsive to the same magnitude of radiation dose.[13,14]

SUMMARY

Drinking water available to rats during a 6-hr gamma radiation exposure was made discriminative by addition of saccharin. Animals irradiated with 30 r or 57 r under these conditions exhibited a marked decrease in their preference for saccharin flavored water during the post-irradiation test. The effect persisted for more than 30 days. It is apparent that animals can learn to discriminate against a normally preferred taste substance when it is associated with radiation exposure.

Approved by:

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89	CG, AFSWP, Hq., Field Command, Sandia Base
90	Assistant Secretary of Defense (Res. and Dev.)
91	Armed Forces Medical Library

92-96	Armed Services Technical Information Agency
97	Armed Forces Institute of Pathology

AEC ACTIVITIES AND OTHERS

98-100	Argonne Cancer Research Hospital
101-106	Argonne National Laboratory
107-108	Atomic Bomb Casualty Commission (APO-182)
109	Atomic Bomb Casualty Commission, Washington
110-112	AEC, Washington
113	Atomic Energy of Canada, Ltd.
114	Australian Atomic Energy Commission
115	Battelle Memorial Institute
116-118	Belgium, Union Miniere du Haut Katanga
119-122	Brookhaven National Laboratory
123	Brush Beryllium Company
124-126	Canadian Joint Staff
127	Carbide and Carbon Chemicals Company (C-31 Plant)
128-129	Carbide and Carbon Chemicals Company (K-25 Plant)
130-135	Carbide and Carbon Chemicals Company (ORNL)
136	Centre d'Etudes pour les Applications de l'Energie Nucleaire
137	Centro Italian Studi Experienze
138-141	Chalk River Project, Canada
142	Chicago Patent Group
143	Columbia University (Failla)
144	Columbia University (Hassialis)
145	Commonwealth X-Ray and Radium Laboratory
146	Consolidated Vultee Aircraft Corporation
147	Division of Raw Materials, Denver
148-149	Dow Chemical Company, Midland
150	Dow Chemical Company, Rocky Flats
151-152	duPont Company, Savannah
153	duPont Company, Wilmington
154	General Electric Company (ANPP)
155-156	General Electric Company, Richland
157	Goodyear Atomic Corporation
158	Harshaw Chemical Corporation
159	Iowa State College
160	Kaiser Engineers
161-162	Knolls Atomic Power Laboratory
163	Lockheed Aircraft Corporation
164-165	Los Alamos Scientific Laboratory
166	Mallinckrodt Chemical Works
167	Massachusetts Institute of Technology (Hardy)
168	Massachusetts Institute of Technology (Kaufmann)
169	Mound Laboratory
170	National Bureau of Standards (Taylor)

171	National Bureau of Standards (Library)
172	National Lead Company of Ohio
173-175	National Research Council, Ottawa
176	New Brunswick Laboratory
177	Newport News Shipbuilding and Drydock Company
178	New York Operations Office
179	North American Aviation, Inc.
180	Nuclear Development Associates, Inc.
181	Oak Ridge Institute of Nuclear Studies
182	Patent Branch, Washington
183-188	Phillips Petroleum Company
189-191	Public Health Service, Washington
192	RAND Corporation
193	Tokyo University
194	United Aircraft Corporation
195-209	United Kingdom Scientific Mission
210	U.S. Geological Survey (Butler)
211	UCLA Medical Research Laboratory
212	University of California Medical Center
213-215	University of California Radiation Laboratory, Berkeley
216-217	University of California Radiation Laboratory, Livermore
218	University of Chicago Radiation Laboratory
219-220	University of Michigan (Gomberg)
221-222	University of Rochester (Technical Report Unit)
223	University of Tennessee (Comar)
224	University of Utah (Bowers)
225	University of Washington, Applied Fisheries Lab.
226	Vitro Corporation of America
227-230	Western Reserve University
231-232	Westinghouse Electric Company
233-257	Technical Information Service, Oak Ridge

USNRDL

258-300	USNRDL, Technical Information Division

DATE ISSUED: 11 January 1955

Naval Radiological Defense Laboratory
USNRDL-TR-19
PERFORMANCE DURING EXPOSURE TO IONIZING RADIATION. PART I. FOOD AND WATER CONSUMPTION OF RATS DURING EXPOSURE TO GAMMA RADIATION. PART II. A CONDITIONED AVERSION TOWARDS SACCHARIN RESULTING FROM EXPOSURE TO GAMMA RADIATION, by J. Garcia, D.J. Kimeldorf, and others. 12 Nov. 1954. 24 p. 6 diag. (14 refs.) UNCLASSIFIED

Rats consumed less water and food, and their body weight decreased during exposure to low intensity gamma radiation. Water consumption became less and less upon repeated

1. Gamma radiation - Biological effects
2. Gamma radiation - Physiological effects
I. Garcia, J.
II. Kimeldorf, D.J.
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